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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/780,643	02/09/2001	Nozer M. Mehta	P/546-239	1033

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EXAMINER
SCHNIZER, HOLLY G

ART UNIT	PAPER NUMBER
1653	8

DATE MAILED: 06/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

FILE COPY

Office Action Summary	Application No.	Applicant(s)	
	09/780,643	MEHTA ET AL.	
	Examiner	Art Unit	
	Holly Schnizer	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *86,87,91-94,96 and 97* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *86,87,91-94,96 and 97* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4&7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Claims

The Preliminary Amendment filed February 9, 2001 (Paper No. 6) has been entered and considered. Claims 1-85, 88-90, 95, and 98-101 have been cancelled. Therefore, Claims 86, 87, 91-94, 96, and 97 are pending and have been considered in this Office Action.

Drawings

The drawings filed July 30, 2001 have been approved by the draftsperson.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 86, 87, 91-94, 96, and 97 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The lack of antecedent basis for "the peptide product" in line 4 of Claim 86 makes the claim confusing because it is unclear whether or not "the peptide product" is in reference to the "amidated peptide product" or another peptide product. The examiner suggests amending the claim to include the phrase --encoding a peptide product-- in the first line after --with an expression vector— in order to make the claim read more clearly

and consistently. Claims 91, 93, and 96 are rejected because they depend from Claim 86 but do not correct its deficiencies.

Likewise, the lack of antecedent basis for "the peptide product" in line 4 of Claim 87 makes the claim confusing because it is unclear whether or not "the peptide product" is in reference to the "amidated peptide product" or another peptide product. The examiner suggests amending line 4 of the claim to read –a peptide product— rather than "the peptide product". Claims 92, 94, and 97 are rejected because they depend from Claim 87 but do not correct its deficiencies.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 86, 91, 93, and 96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koke et al. (Prot. Exp. & Purif. (1991) 2: 51-58; cited in IDS of Paper No. 7) in view of Ray et al. (Biotechnology (Jan. 1993) 11: 64-70, cited in IDS of Paper No. 7).

It appears that prior to Ray et al. salmon calcitonin was produced by chemical synthesis because the lack of carboxyl-amidation of the peptide in prokaryotic systems and the low yields of peptide produced in eukaryotic systems (see Ray et al. paragraph bridging Col. 1 and 2). Ray et al. teaches the expression of a glycine extended salmon calcitonin precursor peptide (sCT-gly) in a culture medium using an expression vector containing a tac promoter (p. 68, Col. 1, lines 6-10 and pages 68-69, under Experimental Protocol, see "plasmid construction"). Ray et al. teaches that the glycine extended peptide was converted to the amidated peptide by contacting the peptide product with oxygen and a reducing agent in the presence of peptidylglycine α-amidating enzyme (α-AE) (see 69, Col. 2, 2nd full paragraph). Ray et al. also teaches that the amidated peptide was purified by using cation exchange chromatography and reverse phase chromatography (see p. 69, Col. 2, 2nd full paragraph). Salmon Calcitonin precursor is a 32 amino acid peptide hormone that requires C-terminal amidation for full biological activity (see Ray et al., 1st line of abstract). Ray et al. teach that calcitonins are used in the treatment of osteoporosis (page 64, col. 1, lines 10-11) and that salmon calcitonin precursor is most frequently used in this therapy (page 64, col. 1, liens 29-30). As expressed in Ray et al., there is a growing importance of

amidated peptide drugs and the need for large-scale efficient production of such proteins.

Ray et al. do not teach the presently claimed expression vector.

Koke et al. teach the construction of vectors for high-level expression in E. coli of phosphatidylinositol-specific phospholipase C (p. 55, col. 1, line 4). The vector with the highest expression of those tested contained a coding region under the control of a lac-tac-tac triple tandem promoter (page 55, col. 1, lines 6-9), as well as a STII signal codon (p. 55, Col. 1, line 14), and a Shine-Dalgarno sequence (p. 55, Col. 1, line 14).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to improve the expression of salmon calcitonin precursor taught in Ray et al. by using the expression vectors taught in Koke et al. One would have had motivation to do so in light of the ability to achieve greater quantities of protein using the multiple promoters of the Koke et al. vector and since Ray et al. express the need to obtain such large scale expression. By using the Koke et al. vectors to express the salmon calcitonin precursor containing a C-terminal glycine more product would be available for the step of amidation of the glycine residue as taught in Ray et al. and consequently more final product could be obtained for use in therapies.

Conclusions

No Claims are allowable.

The methods of Claims 87, 92, 94, and 97 appear to be free of the prior art. While it is standard in the art of protein expression to use the B-strain of E. coli as a

host cell, there is no teaching or suggestion in the art that the BLR host strain would provide significantly greater expression levels than other strains (such as BL-21 or WA837) as shown in the present specification (see Figure 16).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Holly Schnizer whose telephone number is (703) 305-3722. The examiner can normally be reached on Monday through Wednesday from 8 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703 308-0196.

HS

Holly Schnizer
June 2, 2003

Christopher S. F. Low

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